Induction of a Radio-Adaptive Response by Low-dose Gamma Irradiation in Mouse Cardiomyocytes

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One of the most significant occupational hazards to an astronaut is the frequent exposure to radiation. Commonly associated with increased risk for cancer related morbidity and mortality, radiation is also known to increase the risk for cardiovascular related disorders including: pericarditis, hypertension, and heart failure. It is believed that these radiation-induced disorders are a result of abnormal tissue remodeling. It is unknown whether radiation exposure promotes remodeling through fibrotic changes alone or in combination with programmed cell death. Furthermore, it is not known whether it is possible to mitigate the hazardous effects of radiation exposure. As such, we assessed the expression and mechanisms of radiation-induced tissue remodeling and potential radio-adaptive responses of p53-mediated apoptosis and fibrosis pathways along with markers for oxidative stress and inflammation in mice myocardium. 7 week old, male, C57Bl/6 mice were exposed to 6Gy (H) or 5cGy followed 24hr later with 6Gy (LH) ^{137}Cs γ radiation. Mice were sacrificed and their hearts extirpated 4, 24, or 72hr after final irradiation. Real Time - Polymerase Chain Reaction was used to evaluate target genes. Apoptotic genes Bad and Bax, pro-cell survival genes Bcl2 and Bcl2l2, fibrosis gene Vegfa, and oxidative stress genes Sod2 and GPx4 showed a reduced fold regulation change (Bad,-6.18; Bax,-6.94; Bcl2,-5.09; Bcl2l2,-4.03; Vegfa, -11.84; Sod2,-5.97; GPx4*,-28.72; * = Bonferroni adjusted p-value $\leq$ 0.003) 4hr after H, but not after 4hr LH compared to control. Other p53 -mediated apoptosis genes Casp3, Casp9, Trp53, and Myc exhibited down-regulation but did not achieve a notable level of significance 4hr after H. 24hr after H, genetic down-regulation was no longer present compared to 24hr control. These data suggest a general reduction in genetic expression 4hrs after a high dose of γ radiation. However, pre-exposure to 5cGy γ radiation appears to facilitate a radio-adaptive response that mitigates the reduction in genetic expression associated with single high-dose γ radiation exposure. This radio-adaptive response may serve as a potential countermeasure to radiation-induced myocardial remodeling and preserve the cardiovascular health of astronauts; thus, reducing the risks of human space exploration.